

Exhibit A

Claims Pending in U.S. Application No. 10/139,069

1. A method of determining whether a test hepatitis C virus (HCV) has an altered susceptibility to a compound, comprising
 - (a) contacting a test host cell with the compound, wherein the test host cell comprises a test HCV-derived nucleic acid and an indicator gene, the activity of the indicator gene is affected by the activity of the test HCV-derived nucleic acid such that a change in the activity of the test HCV-derived nucleic acid results in a change in the activity of the indicator gene, and the compound directly or indirectly targets the test HCV-derived nucleic acid or a protein it encodes, and
 - (b) detecting the activity of the indicator gene,
wherein a difference in the activity of the indicator gene in the test host cell contacted with the compound relative to the activity of the indicator gene in a reference host cell contacted with the compound and comprising the indicator gene and a reference HCV-derived nucleic acid, the reference HCV-derived nucleic acid being similar to the test HCV-derived nucleic acid but differing therefrom at one or more nucleotides, indicates that the test HCV has an altered susceptibility to the compound.
2. The method of Claim 1 wherein the compound is an anti-viral drug.
3. The method of Claim 2 wherein the anti-viral drug is selected from the group consisting of interferon and ribavirin.
4. The method of Claim 1 wherein the test HCV-derived nucleic acid and the reference HCV-derived nucleic acid are present in viral vectors comprising one or more of the hepatitis C virus genes C, E1, E2, NS2, NS3, NS4A, NS4B, NS5A or NS5B.
5. The method of Claim 1 wherein the test HCV-derived nucleic acid is a patient-derived segment.
6. The method of Claim 5 wherein the patient-derived segment comprises one or more of the hepatitis C virus genes C, E1, E2, NS2, NS3, NS4A, NS4B, NS5A or NS5B.

7. The method of Claim 1 wherein increased activity of the indicator gene in the test host cell relative to the activity of the indicator gene in the reference host cell indicates the test HCV has decreased susceptibility to the compound.
8. A method of determining whether a compound affects a hepatitis C virus (HCV), comprising
 - (a) contacting a host cell with the compound, wherein the host cell comprises an HCV-derived nucleic acid from the virus and an indicator gene, the activity of the indicator gene is affected by the activity of the HCV-derived nucleic acid such that a change in the activity of the HCV-derived nucleic acid results in a change in the activity of the indicator gene, and the compound directly or indirectly targets the HCV-derived nucleic acid or a protein it encodes, and
 - (b) detecting the activity of the indicator gene,wherein a difference in the activity of the indicator gene in the host cell contacted with the compound relative to the activity of the indicator gene in the host cell not contacted with the compound indicates that the compound affects the virus.
9. The method of Claim 8 wherein the compound is an anti-viral drug.
10. The method of Claim 9 wherein the an anti-viral drug is selected from the group consisting of interferon and ribavirin.
11. The method of Claim 8 wherein the HCV-derived nucleic acid is present in a viral vector comprising one or more of the hepatitis C virus genes C, E1, E2, NS2, NS3, NS4A, NS4B, NS5A or NS5B.
12. The method of Claim 8 wherein the HCV-derived nucleic acid is a patient-derived segment.
13. The method of Claim 12 wherein the patient-derived segment comprises one or more of the hepatitis C virus genes C, E1, E2, NS2, NS3, NS4A, NS4B, NS5A or NS5B.
14. The method of Claim 8 wherein increased activity of the indicator gene in the test host cell relative to the activity of the indicator gene in the reference host cell indicates the test HCV has decreased susceptibility to the compound.

15. A method of determining whether a patient infected with hepatitis C virus is likely to be susceptible to treatment with an anti-hepatitis C compound comprising
 - (a) contacting a test host cell with the compound, wherein the test host cell comprises a patient-derived viral segment and an indicator gene, the activity of the indicator gene is affected by the activity of the patient-derived viral segment such that a change in the activity of the patient-derived viral segment results in a change in the activity of the indicator gene, and the compound directly or indirectly targets the patient-derived viral segment or a protein it encodes, and
 - (b) detecting the activity of the indicator gene, wherein an increase in the activity of the indicator gene in the test host cell contacted with the compound relative to the activity of the indicator gene in a reference host cell contacted with the compound and comprising the indicator gene and a reference viral segment, the reference viral segment being similar to the patient-derived viral segment but differing therefrom at one or more nucleotides, indicates that the patient is less likely to be susceptible to treatment with the compound.
16. The method of Claim 15 wherein the compound is an anti-viral drug.
17. The method of Claim 16 wherein the anti-viral drug is selected from the group consisting of interferon and ribavirin.
18. The method of Claim 15 wherein the patient-derived viral segment is present in a viral vector comprising one or more of the hepatitis C virus genes C, E1, E2, NS2, NS3, NS4A, NS4B, NS5A or NS5B.
19. The method of Claim 15 wherein the indicator gene is integrated into the host cell genome.
20. The method of Claim 15 wherein the patient-derived viral segment comprises one or more of the hepatitis C virus genes C, E1, E2, NS2, NS3, NS4A, NS4B, NS5A or NS5B.